REMARKS

Claims 1-13 are pending. Support for the amendments to claim 1 can be found at page 4, lines 11-12 and page 3, lines 11-13. Support for claims 7-13 can be found in the specification at page 3, lines 39-40; page 4, lines 11-13; page 4, lines 11-16; page 3, line 12; page 3, line 19; page 3, line 20; and page 2, lines 42-43, respectively.

The examiner has indicated that applicant has not filed a certified copy of the priority document. However, the priority document concerned (German application 199 30 454.8) was submitted to the International Bureau (see enclosed Notification). The International Bureau should have forwarded the priority document to the USPTO. Applicants submit herewith a verified translation of said priority document.

Claims 1-3 stand rejected under 35 U.S.C. 102(b) as being anticipated by Krape et al. (WO 99/00131). Applicants respectfully traverse this rejection.

Krape et al. describes two alternative ways for preparing solid state dispersions of paroxetine. In the so-called "solution method," the active ingredient is dispersed in a water-soluble carrier by dissolving a physical mixture containing the active ingredient and the pharmaceutically acceptable carrier in a common organic solvent and then removing the solvent by evaporation. While Krape et al. contains no explicit teaching to use carriers comprising a completely synthetic polymer having a glass transition temperature of >90°C in the anhydrous state (as required by present claim 1), PVP 29/32 K is used in examples 5 and 6. This polyvinylpyrrolidone has a glass transition temperature higher than 90°C. However, Krape et al.'s examples 5 and 6 show that if such a polymer is used, the solution method yields preparations which are <u>not</u>

substantially free of volatile organic solvents. In fact, the preparations obtained in accordance with examples 5 and 6 contain 4% by weight of methanol and 14% by weight of ethanol, respectively (please note that the heading of example 6 erroneously refers to PEG-8000 while the text of example 6 clearly states that the polyvinylpyrrolidone was used). Only if PEG-8000 which is a waxy substance and therefore cannot have a glass transition temperature of >90°C is used, preparations may be obtained which do not contain residual organic solvent (compare example 2).

In contrast thereto, the preparations according to present claim 1 as amended are substantially free of volatile organic solvent and comprise a completely synthetic polymer having a glass transition temperature >90°C.

The second process to which Krape et al. refers is the so-called fusion or "melt" process. This process involves contacting a water-soluble pharmaceutically acceptable polymeric carrier with a paroxetine free base, heating the mixture to form a molten homogeneous melt and contacting said melt with hydrogen chloride to form the hydrochloride of paroxetine, and cooling the melt to form the solid state dispersion. Krape et al. explicitly states on page 4, lines 17 to 24 that the pharmaceutically acceptable carrier has a melting point significantly lower than that of anhydrous paroxetine hydrochloride which allows said process to be performed at temperatures substantially lower than the melting point of paroxetine hydrochloride. Taking into account that the melting point of anhydrous paroxetine hydrochloride is about 118°C, it is clear that Krape et al. does not teach using a polymer having a glass transition temperature of >90°C for said fusion method. This is further corroborated by the

examples. Indeed, all examples which refer to said fusion method (examples 1, 14, 15 and 16) use PEG-8000 which does not have a glass transition temperature of >90°C but is a waxy substance.

Therefore, the subject-matter of the presently amended claims is novel over Krape et al.

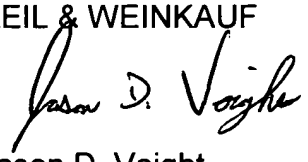
The subject-matter of the presently amended claims is also non-obvious over Krape et al. As far as Krape et al. is concerned, only the fusion method appears to be suitable for obtaining preparations which are free of volatile organic solvent. Using this method the person of ordinary skill in the art would, however, by confined to polymeric carriers which have a rather low melting point such as polyethylene glycols. The skilled person would, however, not have been motivated to use a polymer having a glass transition temperature of >90°C since this would not allow compliance with the requirement of conducting the process at temperatures substantially lower than the melting point of paroxetine hydrochloride. As mentioned above, Krape et al. explicitly requires that the pharmaceutically acceptable carrier has a melting point significantly lower than that of anhydrous paroxetine hydrochloride.

Claims 4-6 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Krape et al. in view of Craig et al. (WO 00/32593) and further in view of Patel et al. (US 6,248,363). Applicants respectfully traverse this rejection. Craig et al. was published June 8, 2000 and filed November 30, 1999. Patel et al. was filed November 23, 1999. The present application claims a priority date of July 2, 1999. Therefore, in view of the enclosed verified translation of the priority document, it is urged that neither Craig et al.

nor Patel et al. is prior art with respect to the present application.

Please charge any shortage in fees due in connection with the filing of this paper, including Extension of Time fees to Deposit Account No. 11.0345. Please credit any excess fees to such deposit account.

Respectfully submitted,
KEIL & WEINKAUF



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IN THE SPECIFICATION

At page 1, after the title, insert:

This application is a 371 of PCT/EP00/05848, filed June 23, 2000.

IN THE CLAIMS

1. (currently amended) A solid or semisolid preparation which is substantially free of volatile organic solvent, said preparation comprising ~~of~~ paroxetine or one of its physiologically acceptable salts in the form of a molecular dispersion ~~of~~ ~~paroxetine~~ in a pharmaceutically acceptable matrix material which comprises a completely synthetic polymer having a glass transition temperature of >90°C in the anhydrous state.

2. (currently amended) ~~A~~ The preparation ~~as claimed in~~ of claim 1, comprising paroxetine hydrochloride.

3. (currently amended) ~~A~~ The preparation ~~as claimed in claim 1~~ of claim 2 having an active ingredient release of at least 80% after 30 min.

4. (currently amended) A process for producing a preparation as claimed in claim 1, which process comprises the paroxetine or one of its salts and the matrix material being mixed to give a homogeneous melt in an extruder and subsequently being shaped.

5. (currently amended) ~~A~~ The process ~~as claimed in~~ of claim 4 for producing a paroxetine hydrochloride preparation, wherein paroxetine is processed with ammonium chloride and the matrix materials to give a homogeneous melt.

6. (currently amended) A The process ~~as claimed in~~ of claim 5, wherein amorphous paroxetine or one of its physiologically acceptable salts is employed.

7. (new) The process of claim 4, wherein the melt is produced at a temperature in

the range of 80 to 150°C.

8. (new) The process of claim 4, further comprising applying a vacuum to the extruder while the paroxetine or one of its salts and the matrix material are being mixed if solvents are present therein.

9. (new) The preparation of claim 1, which is also free of water.

10. (new) The preparation of claim 1, wherein the polymer has a glass transition temperature of >90°C to 110°C in the anhydrous state.

11. (new) The preparation of claim 1, wherein the polymer is a copolymer of N-vinylpyrrolidone and vinyl acetate.

12. (new) The preparation of claim 11, wherein the polymer is copovidone.

13. (new) The preparation of claim 1, which is a solid.

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

To:

GOLDSCHEID, Bettina
BASF Aktiengesellschaft
D-67056 Ludwigshafen
ALLEMAGNE

Patente, Marken u. Lizenzen
16. AUG. 2000

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

Date of mailing (day/month/year) 23 August 2000 (23.08.00)	
Applicant's or agent's file reference 0480/001221	**IMPORTANT NOTIFICATION**
International application No. PCT/EP00/05848 ✓	International filing date (day/month/year) 23 June 2000 (23.06.00) ✓
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 02 July 1999 (02.07.99) ✓
Applicant KNOLL AKTIENGESELLSCHAFT et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An **asterisk(*)** appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The **letters "NR"** appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
02 July 1999 (02.07.99) ✓	199 30 454.8 ✓	DE	25 July 2000 (25.07.00)

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Céline Faust
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